



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,991	11/20/2001	Gregory Luedtke	219002029100	1704

25225 7590 10/06/2003
MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER

CHANG, CELIA C

ART UNIT	PAPER NUMBER
----------	--------------

1625

DATE MAILED: 10/06/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/989,991

Applicant(s)

LUEDTKE ET AL.

Examiner

Celia Chang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-9, 11, 12, 39-61 and 63-68 is/are pending in the application.
- 4a) Of the above claim(s) 2, 11 and 64-67 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1, 3-9, 12, 39-61, 63 and 68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. Amendment and response filed by applicants in Paper No. 13 dated July 9, 2003 have been entered and considered carefully. Claims 1-9, 11-12, 39-61, 63-68 are pending. Please note that claims 2-9, 11-34, 40-68 were withdrawn from consideration in the previous office action.

Applicants have been reminded for the lack of election of a single disclosed method thus claims 64-67 being drawn to multiple ingredient composition or method mediated i.e. both too much and too little p-38- α kinase stayed withdrawn for being drawn to the nonelected invention. Claim 2 and 11 stayed withdrawn since these claims now do not read on the base claim wherein X is bicyclo ring of claim 1 and the non-interfering groups lacks antecedent basis as being joined.

Claims 3-9, 12, 39-61, 63 and 68 reading on the *newly* amended claims 1 will be considered together with the amended claims. Consideration of claims 3-9, 12, 39-61, 63 and 68 which are now made dependent on *newly* amended base claims would be necessitated by the amendments.

2. The rejection of claims 1, 10, 35-38 under 35 USC 112 second paragraph is maintained for reason of record and now applicable to the amended claims 3-9, 12, 39-61, 63, 68 whenever the rejected terms noninterfering group, linker and spacer was employed.

Applicants argued that the "non-interfering groups" is not indefinite because as it was found on page 5, lines 7-25, the structure is *irrelevant*. A survey of page 5, lines 7-25 indicated that no description of "what" such groups may be but any group which resulted in a compound tested positive to the p-38- α kinase activity can be included. Please note that a claim defines the meets and bounds of a material, which in the instant case is a group of compounds meeting the Markush elements. It is unclear how one determines "what" is the claimed compound since the compound must be made and tested to be -p38 positive and without bioassay *after* a compound is made, one having ordinary skill in the art reading the claims encompassed by "noninterfering groups" based on the description of page 5, lines 7-25, can not ascertain whether a compound is *within* the claim or *not within* the claim. A Markush element must define "what" is the element

Art Unit: 1625

not how it can be tested, especially, in the instant biological/chemical art a high degree of unpredictability is well recognized.

Applicants argued that "it is not clear to applicants why *each of W and X is a spacer of 2-6Å* would be considered indefinite" since bond length can be delineated from handbooks. Please note that the term W and X is spacer when i and j can be zero is self conflicting since a spacer by definition is an element that created a space. If it is not existing and the space is still 2-6Å what does it mean? Are the claims being drawn to material there is a "space", a void or hole? Or are the claims drawn to compounds with an element which has certain size? Besides, how does this 2-6Å being measured, by adding the chain length of the carbon atoms? side chains? rings? What is included in the calculation what is not?

Further the term "spacer" "linker" or "noninterfering substituents" as now amended and argued to be "less important" (p.5, line 27 specification) or "not relevant" (p.11 7th line from bottom, response) i.e. such elements are not required by the claims together with the removal of the limitation of "L linked to Ar.....4-25Å" necessitated the new grounds of rejections.

As noted in MPEP §2111, during patent examination, claims are given their broadest reasonable interpretation consistent with the specification. Terms of the claims are given their customary meaning of the art and no limitation should be read from the specification into the claims In re Paulsen 31 USPQ2d 1671, In re Priest 199 USPQ 11.

The term "spacer" broadly can be interpreted to include the meaning as polylysine (see US 2003/0109682, p.12 section [1065]). The term "linker" after deletion of ambiguous size limitation broadly can be interpreted to include the meaning as bifunctional linker as found in US2002/0160388 p.26 section [0226]. The term "noninterfering group" would include unlimited polymeric linker/conjugate delineated supra. Such definition lacks descriptive support of the specification and are considered to contain NEW MATTER thus a 112 first paragraph rejection will follow.

The term "heteroalkyl" "heteroalylene" "heteroalenylene" "heteroalynylene" of claims 44, 47, 51, 58, 60 are indefinite and confusing. Please note that in the specification on pages 6-7, it was defined that "...1-2 O, S or N.....backbone residue". Since the linker, spacer and substituents are not essential and can be in any position and any type, thus no attachment

limitation, what does this linkage describe? Clarification is required. Further, on page 7, lines 3-5, it was defined that heteroalkyl include "aromatic or heteroaromatic systems". Although applicants act as his or her own lexicographer to specifically define a term of a claim of its meaning, the written description must clearly redefine the "claim term", such description must be consistent with the ordinary meaning of the term and non-conflicting through out the specification. The terms are indefinite because the specification does not clearly describe what they are.

3. Claims 1, 3-9, 12-38, 40-63, 68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The explanation of NEW MATTER as delineated supra in section 2 is hereby incorporated by reference.

Further, R2 or R3 being halogen, OR or alkyl lacks antecedent basis i.e. NEW MATTER since the substituents being supported by the specification found in examples 1-6 are limited to chloro, fluoro, methoxy or acetylamino.

4. By given the term with the broadest reasonable meaning guided by art and the description of the specification that substituents are not relevant together with attorney's allegation that only the *essential feature* is needed to claim the compounds (see p.11 response and p.5 specification essential feature is 2- or 3-indole), the following rejections are made wherein the claims include the mandatory indole with CO with any linking group at 2- or 3- position, a spiran X and an aryl linked in any position with any linker.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1625

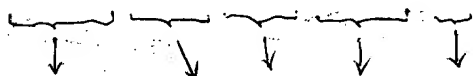
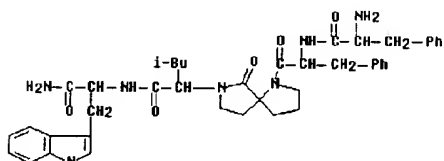
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims, 1, 3-9, 12, 40-61, 63, 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ward et al. US 5,166,136 in view of Rubini.

Determine The Scope and Content of the Prior Art (MPEP 2144.01)

Ward et al.'136 disclosed anti-inflammatory compounds wherein a structural closely related species is found in col. 24 example 35 (see CA structure attached). Since this compound is useful in treating inflammation it has anti-inflammatory response i.e. the claimed requirement since the position or type of linker or spacer are not relevant. The compounds have an indole with 3- substituents having a carbonyl group, a spiran ring and linker to an aryl group i.e.



3-substituted L1 X L2 Ar
indole

Ascertain The Differences Between the Prior Art and the Claim (MPEP 2144.02)

Ward et al. '136 disclosed all the elements of the claims **except** instead of a methylene on the spiran, Ward '136 has an oxo substitution. Rubini taught that methyleneamine linker is an amide bond surrogate with analogous bonding arrangement (see whole article) and suggested that such surrogate is desirable since the modification would enhance metabolic stability of a known drug.

Art Unit: 1625

Rational and motivation for finding of prima facie obviousness (MPEP 2144.03)

One having ordinary skill in the art in possession of the above references would be motivated to modify the known compound with an amide bond surrogate i.e. replace the oxo with a methylene, **because** it was suggested by the art that such modification would be expected to improve metabolic stability in biological active compounds.

5. The rejections of claims 1, 10, 35-38 under 35 USC 102(f) or (b) over CA 137, 118, 123 or 128 are dropped in view of the amendment of claims to the particular spiran.

Claim 39 stayed objected to for depending on rejected base claims.

6. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

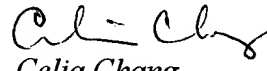
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman, can be reached on (703) 308-4968. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

OACS/Chang
Oct. 1, 2003


Celia Chang
Primary Examiner
Art Unit 1625